Remarks

I. Support For The Amendment

Claims 7, 9, 17-23 and 25-29 are pending. Claims 24 and 30 are canceled in this amendment. Claim 7 has been amended to specify that the claimed antibody or antibody fragments bind the FDF03-S1 polypeptide of SEQ ID NO: 6, but do not bind the FDF03 polypeptide of SEQ ID NO: 2.

Applicants submit that the amendment to claim 7 is fully supported by the specification as filed. In particular, the specification teaches that the FDF03-S1 protein of the present invention is homologous to the previously known monocyte-derived protein known as "FDF03" (page 5, lines 14-19 and paragraph bridging pages 6-7). Indeed, the substantial sequence homology between these two proteins is illustrated by the alignment of their amino acid sequences that is presented on page 7. However, the specification explicitly highlights important structural and functional differences between FDF03 and FDF03-S1 (see page 6, line 27 to page 7, line 12). The specification describes preparation of antibodies on page 18, line 21 – page 21, line 2 and then describes how the resulting antibodies may be used, which uses are instructive of what Applicants intended regarding their cross-reactivity to FDF03. In particular, on page 21, lines 3-7 of the specification, Applicants describe using the antibodies "to isolate and purify" immunogenic components by immunoaffinity chromatography, to "screen expression libraries" for particular expression products, and "as probes to distinguish tissue and cell type distribution." Similarly, page 21, lines 20-24 describes the use of antibodies specific for a particular component disclosed in the application "in clinical settings for the qualitative or quantitative diagnosis, i.e., detection of specific components in a biological sample." Each of these explicitly described uses for antibodies that specifically bind to FDF03-S1 clearly implies that the Applicants contemplated using antibodies that do not cross-react with FDF03.

In view of the disclosure discussed above, it would have been clear to one skilled in the art that, as of the filing date, Applicants contemplated the production of antibodies to the FDF03-S1 polypeptide of SEQ ID NO: 6 that would not cross-react with the FDF03 polypeptide of SEQ ID NO: 2. Since the lack of cross-reactivity of the claimed antibodies with SEQ ID NO:2 is implicitly supported by the specification, amended claim 7 satisfies the written description requirement.

II. Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 18, 24 and 30 stand rejected as allegedly indefinite. With respect to the indefiniteness rejection of claim 18, Applicants respectfully traverse.

The Examiner has maintained the objection to the term "antibody half molecule" in claim 18. In particular, the Examiner argues that the claims must be given the "broadest reasonable interpretation consistent with the specification" and that said interpretation in the present instance "would encompass any half of an antibody e.g. the half antibody molecule comprising only the Fc region." (Office Action p. 3). Applicants disagree.

As the Examiner correctly states, claims are to be given the broadest reasonable interpretation consistent with the specification (MPEP 2173.04). The only interpretation of the term "antibody half molecule" that is consistent with the present specification is found in the reference cited (p. 20) and incorporated (p. 3, lines 2-3) by the specification, as detailed below.

> Page 20 of the Specification, last line, to page 21, first line, reads as follows:
>
> "The use and generation of antibody fragments is also well-known, e.g., Fab fragments: Tijssen, 1985, *Practice and Theory of Enzyme immunoassays*, Elsevier, Amsterdam; Fv fragments: Hochman et al., 1973 *Biochemistry* 12:1130; Sharon et al., 1976, *Biochemistry* 15:1591; Ehrlich et al., U.S. Pat. No., 4,355,023; and antibody half molecules: Auditore-Hargreaves, U.S. Pat. No. 4,470,925. These also may be useful in immunoassays." (emphasis added).

U.S. Patent No. 4,470,925 ("the '925 patent") defines an "antibody half molecule" consistently throughout as follows:

> "The half-molecules of this invention are substantially pure immunoglobulin heavy chain-light half-molecules having the structure R—S—X, where R is H_1L_1 and X is either hydrogen (H) or SO_3^{θ}. They are prepared by selectively cleaving an immunoglobulin molecule into its heavy chain-light chain half molecules by sulfitolysis or by reduction of the inter-heavy chain disulfide linkage." (column 2, lines 26-33) (emphasis added).

This definition of "antibody half molecule" is relied upon consistently throughout the '925 patent. The present specification incorporates the '925 patent at page 3, lines 2-3. It also specifically cites the '925 for the definition of "antibody half molecule". Thus, the Examiner's concern that the term would encompass "any half of an antibody" is unfounded. Applicants respectfully request that this rejection be reconsidered and withdrawn.

The Examiner also objects to the term "unit dose" in claims 24 and 30. This rejection has been obviated by the cancellation of those claims.

Applicants respectfully request that the indefiniteness rejections be reconsidered and withdrawn.

III. The Rejection Under 35 U.S.C. § 102 Should Be Withdrawn

The Examiner has maintained the rejection of claims 7, 9 and 17-30 under 35 U.S.C.§ 102(b) as being anticipated by Adema[1] as evidenced by Bost[2] and Bendayan[3]. Applicants respectfully traverse.

Adema discloses and claims the protein FDF03, a protein expressed in monocytes. The FDF03 protein is also disclosed in the present application as SEQ ID NO:2. The invention of the present application is a homologous protein termed FDF03-S1 by Applicants, and is directly compared to the FDF03 protein of Adema at page 7 of the specification.

The Examiner's argument is, essentially, that since the amino acid sequences of the FDF03 protein disclosed as SEQ ID NO: 2 in Adema and of the FDF03-S1 protein disclosed as SEQ ID NO:6 of the present application are 80.4% identical, the antibodies taught in Adema would likely cross-react with the FDF03-S1 protein of SEQ ID NO:6. Therefore, according to the Examiner, the Adema antibodies anticipate Applicants claims. Applicants submit that this argument has been obviated in view of the amendment to claim 7, which specifies that the claimed antibodies do not bind the FDF03 polypeptide of SEQ ID NO: 2.

Moreover, the preparation of antibodies defined by amended claim 7 was enabled by the specification, as established by the evidence provided in the accompanying Declaration under 37 C.F.R. § 1.132 of Joseph H. Phillips ("Phillips Declaration"). For example, as illustrated by the sequence comparison on page 7 of the specification and explained in detail in the accompanying Phillips Declaration, the extracellular stock region of the FDF03-S1 protein is significantly different from the stock region of FDF03 (Phillips Declaration ¶ 6). As such, standard techniques in monoclonal antibody production technology can be used to generate

---

[1] Adema *et al.*, publication no. WO 98/24906.

[2] Bost, K.L. and Pascual, D.W., *Immunological Investigations 17(6&7)*: 577-586 (1988).

[3] Bendayan, M., *J. Histochemistry and Cytochemistry 43(9)*: 881-886 (1995).

antibodies against the S1 stock region that recognize the FDF03-S1 protein and not the FDF03 protein of Adema (Phillips Declaration ¶ 6 and ¶ 9).

Alternately, antibodies can be raised against the entire extracellular region of the FDF03-S1 protein, and the resultant antibody population can be screened for antibodies that recognize the FDF03-S1 protein but do not recognize the FDF03 protein (Phillips Declaration ¶¶ 8-9). Indeed, as shown in Table 1 of the Phillips Declaration, seven of thirteen antibodies that were raised against the extracellular region of mouse FDF03-S1 were found to specifically recognize mouse FDF03-S1, but not mouse FDF03 (MB452-2A8, MB452-3A9, MB452-4E9, MB452-5C3, MB452-10E5, MB452-11E2 and MB452-11F5; Phillips Declaration ¶ 8).

In view of the amended claims and the accompanying Phillips Declaration and discussion, Applicants respectfully request that this rejection be reconsidered and withdrawn.

CONCLUSION

Applicants submit that claims 7, 9, 17-23 and 25-29, as amended, are clear and definite and are free of the prior art. Accordingly, reconsideration of the rejections and allowance of the claims at an early date are earnestly solicited.

If the undersigned can be of assistance in advancing the application to allowance, please contact the undersigned at the number set forth below.

Respectfully submitted,

SCHERING-PLOUGH CORPORATION

Melodie Henderson
Attorney for Applicants
Reg. No. 37,848

May 21, 2007
Schering-Plough Corporation
Patent Department
Mail Stop K-6-1, 1990
2000 Galloping Hill Road
Kenilworth, NJ 07033-0530
Telephone No. (908) 298-7482
Facsimile No. (908) 298-5388